

09/811,870 SEARCH STRATEGY

(FILE 'HOME' ENTERED AT 15:35:32 ON 13 NOV 2003)

FILE 'CAPLUS' ENTERED AT 15:35:40 ON 13 NOV 2003

L1           E COLE P A/AU 25  
10 S (E3 OR E48 OR E49 OR E50 OR E51 OR E54) AND (KINASE AND INHIB  
E PARANG K/AU 25  
L2           4 S (E3 OR E4 OR E5) AND (KINASE AND INHIBITOR)  
E ABLOOGU A/AU 25  
L3           4 S (E1 OR E2 OR E4) AND (KINASE AND INHIBITOR)  
E KOHANSKI R A/AU 25  
L4           7 S (E3 OR E4 OR E5 OR E6 OR E7) AND (KINASE AND INHIBITOR)  
E COURTNEY A/AU 25  
L5           1 S (E3 OR E5 OR E11 OR E12) AND (KINASE AND INHIBITOR)

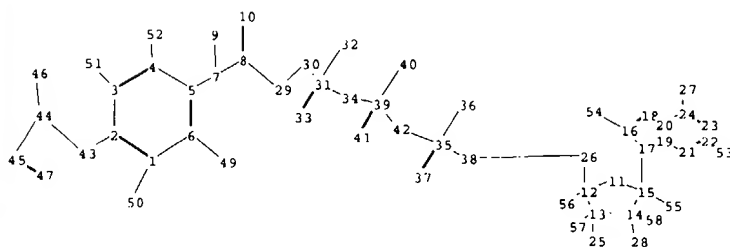
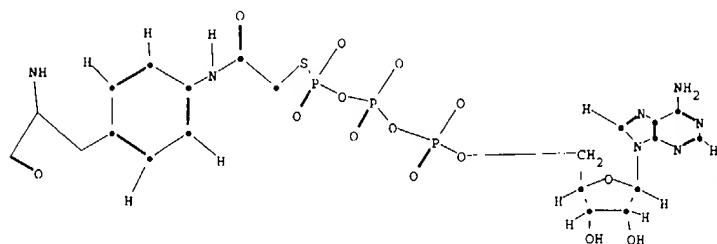
FILE 'MEDLINE, AGRICOLA, CAPLUS, BIOSIS, EMBASE, WPIDS' ENTERED AT  
15:40:05 ON 13 NOV 2003

L6           105 S BISUBSTRATE (W) INHIBITOR  
L7           54 S L6 AND (KINASE)  
L8           19 DUP REM L7 (35 DUPLICATES REMOVED)

=>

	Type	L #	Hits	Search Text	DBs	Time Stamp
1	BRS	L1	2	5990094.pn.	USPAT; US-PGP UB; EPO; JPO; DERWE	2003/11/13 15:28
2	BRS	L2	6944	cole.in. or parang.in. or abloogu.in. or kohanski.in. or courtney.in.	USPAT; US-PGP UB; EPO; JPO; DERWE	2003/11/13 15:28
3	BRS	L3	20	l2 and ((bisubstrate or inhibitor) and kinase)	USPAT; US-PGP UB; EPO; JPO; DERWE	2003/11/13 15:33
4	BRS	L4	10	bisubstrate adj inhibitor	USPAT; US-PGP UB; EPO; JPO; DERWE	2003/11/13 15:33
5	BRS	L5	8	l4 and kinase	USPAT; US-PGP UB; EPO; JPO; DERWE	2003/11/13 15:33

C:\Program Files\Stnexp\Queries\compound2.str



chain nodes :

7 8 9 10 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44  
45 46 47 49 50 51 52 53 54 55 56 57 58

ring nodes :

1 2 3 4 5 6 11 12 13 14 15 16 17 18 19 20 21 22 23 24

chain bonds :

1-50 2-43 3-51 4-52 5-7 6-49 7-8 7-9 8-10 8-29 12-26 12-56 13-25 13-57 14-28  
14-58 15-17 15-55 16-54 22-53 24-27 26-38 29-30 30-31 31-32 31-33 31-34 34-39  
35-38 35-36 35-37 35-42 39-41 39-40 39-42 43-44 44-45 44-46 45-47

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 11-12 11-15 12-13 13-14 14-15 16-17 16-18 17-19 18-20  
19-20 19-21 20-24 21-22 22-23 23-24

exact/norm bonds :

5-7 7-8 8-10 11-12 11-15 12-13 13-14 13-25 14-15 14-28 15-17 16-17 16-18 17-19  
18-20 24-27 29-30 30-31 31-32 31-33 31-34 34-39 35-38 35-36 35-37 35-42 39-41  
39-40 39-42 44-46 45-47

exact bonds :

1-50 2-43 3-51 4-52 6-49 7-9 8-29 12-26 12-56 13-57 14-58 15-55 16-54 22-53  
26-38 43-44 44-45

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6 19-20 19-21 20-24 21-22 22-23 23-24

isolated ring systems :

containing 1 :

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom  
12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 21:Atom  
22:Atom 23:Atom 24:Atom 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 30:CLASS  
31:CLASS 32:CLASS 33:CLASS 34:Atom 35:CLASS 36:CLASS 37:CLASS 38:Atom 39:CLASS  
40:CLASS 41:CLASS 42:CLASS 43:CLASS 44:CLASS 45:CLASS 46:CLASS 47:CLASS 49:CLASS  
50:CLASS 51:CLASS 52:CLASS 53:CLASS 54:CLASS 55:CLASS 56:CLASS 57:CLASS 58:CLASS

09/891865 SEARCH STRATEGY

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1652DJS

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America  
NEWS 2 "Ask CAS" for self-help around the clock  
NEWS 3 SEP 09 CA/CAPLUS records now contain indexing from 1907 to the  
present  
NEWS 4 AUG 05 New pricing for EUROPATFULL and PCTFULL effective  
August 1, 2003  
NEWS 5 AUG 13 Field Availability (/FA) field enhanced in BELLSTEIN  
NEWS 6 AUG 18 Data available for download as a PDF in RDISCLOSURE  
NEWS 7 AUG 18 Simultaneous left and right truncation added to PASCAL  
NEWS 8 AUG 18 FROSTI and KOSMET enhanced with Simultaneous Left and Right  
Truncation  
NEWS 9 AUG 18 Simultaneous left and right truncation added to ANABSTR  
NEWS 10 SEP 22 DIPPR file reloaded  
NEWS 11 SEP 25 INPADOC: Legal Status data to be reloaded  
NEWS 12 SEP 29 DISSABS now available on STN  
NEWS 13 OCT 10 PCTFULL: Two new display fields added  
NEWS 14 OCT 21 BIOSIS file reloaded and enhanced  
NEWS 15 OCT 28 BIOSIS file segment of TOXCENTER reloaded and enhanced  
  
NEWS EXPRESS OCTOBER 01 CURRENT WINDOWS VERSION IS V6.01a, CURRENT  
MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),  
AND CURRENT DISCOVER FILE IS DATED 23 SEPTEMBER 2003  
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NEWS WWW CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 13:11:16 ON 13 NOV 2003

=> file registry

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 13:11:27 ON 13 NOV 2003

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Property values tagged with IC are from the ZIC/VINITI data file  
provided by InfoChem.

STRUCTURE FILE UPDATES: 12 NOV 2003 HIGHEST RN 616193-58-9  
DICTIONARY FILE UPDATES: 12 NOV 2003 HIGHEST RN 616193-58-9

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

09/891865 SEARCH STRATEGY

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=>

Uploading compound2.str

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 13:12:04 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 1 TO ITERATE

100.0% PROCESSED 1 ITERATIONS 0 ANSWERS  
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 1 TO 80  
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 sss full

FULL SEARCH INITIATED 13:12:32 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 5 TO ITERATE

100.0% PROCESSED 5 ITERATIONS 1 ANSWERS  
SEARCH TIME: 00.00.01

L3 1 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	148.55	148.76

FILE 'CAPLUS' ENTERED AT 13:12:38 ON 13 NOV 2003  
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FILE COVERS 1907 - 13 Nov 2003 VOL 139 ISS 20  
FILE LAST UPDATED: 12 Nov 2003 (20031112/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3

L4 2 L3

=> d l- ibib abs hitstr

YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN  
ACCESSION NUMBER: 2001:713377 CAPLUS

## 09/891865 SEARCH STRATEGY

DOCUMENT NUMBER: 135:253738  
TITLE: Bisubstrate inhibitors of kinases  
INVENTOR(S): Courtney, Aliya; Cole, Philip A.; Parang, Keykavous;  
Abloogu, Ararat; Kohanski, Ron  
PATENT ASSIGNEE(S): Johns Hopkins University, USA  
SOURCE: PCT Int. Appl., 39 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001070770	A2	20010927	WO 2001-US8886	20010321
WO 2001070770	A3	20020704		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 2002031820	A1	20020314	US 2001-811870	20010321

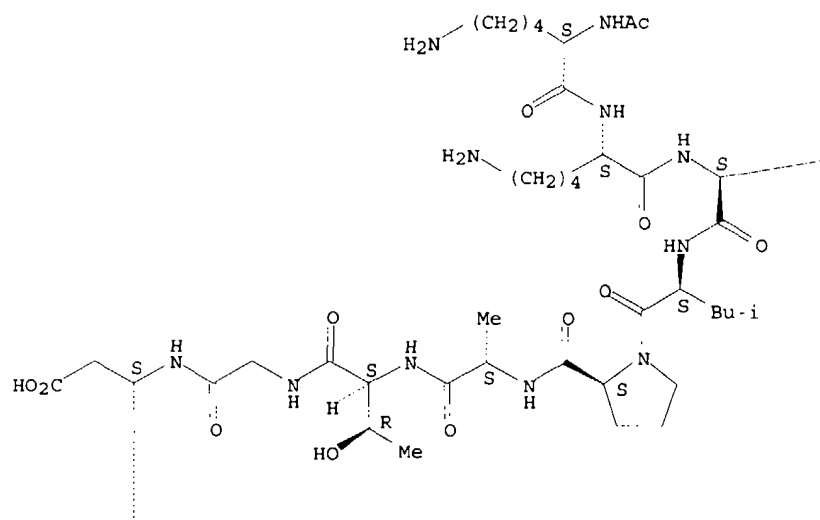
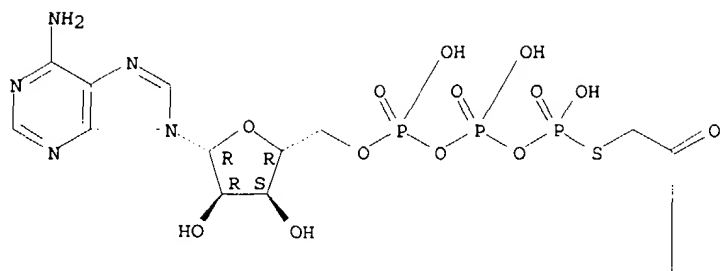
PRIORITY APPLN. INFO.: US 2000-190799P P 20000321

AB Protein kinase inhibitors have applications as anti-cancer therapeutic agents and biol. tools in cell signalling. Potent and selective bisubstrate inhibitors for the insulin receptor tyrosine kinase are based on a phosphoryl transfer mechanism involving a dissociative transition state. One such inhibitor is synthesized by linking ATP.gamma.S to a peptide substrate analog via a two-carbon spacer. The compd. is a high-affinity competitive inhibitor against both nucleotide and peptide substrate and shows a slow off-rate. A crystal structure of this inhibitor bound to the tyrosine kinase domain of the insulin receptor confirms the key design features inspired by a dissociative transition state, and reveal that the linker takes part in the octahedral coordination of an active site Mg2+ ion. A Kemptide-ATP.gamma.S compd. was also prepd. This compd. was an inhibitor of protein kinase A.

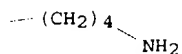
IT 329783-44-0P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(insulin receptor tyrosine kinase inhibitor; bisubstrate inhibitors of kinases)

RN 329783-44-0 CAPLUS  
CN L-Aspartic acid, N2-acetyl-L-lysyl-L-lysyl-L-lysyl-L-leucyl-L-prolyl-L-alanyl-L-threonylglycyl-L-.alpha.-aspartyl-4-[[6-(5'-adenylyloxy)-4,6-dihydroxy-4,6-dioxo-1-oxo-5-oxa-3-thia-4,6-diphosphahex-1-yl]amino]-L-phenylalanyl-L-methionyl-L-asparaginy-L-methionyl-L-seryl-L-prolyl-L-valylglycyl- (9CI) (CA INDEX NAME)

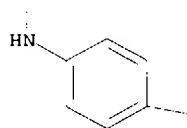
Absolute stereochemistry.



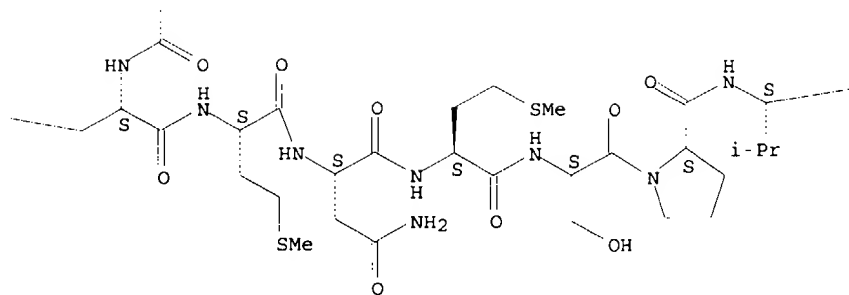
PAGE 1-C



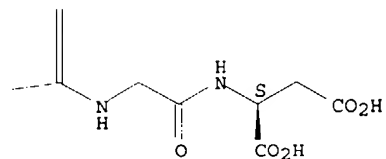
PAGE 2-A



PAGE 2-B



PAGE 2-C



L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:37882 CAPLUS

DOCUMENT NUMBER: 134:218831

TITLE: Mechanism-based design of a protein kinase inhibitor  
 AUTHOR(S): Parang, Keykavous; Till, Jeffrey H.; Ablooglu, Ararat J.; Kohanski, Ronald A.; Hubbard, Stevan R.; Cole, Philip A.

CORPORATE SOURCE: Department of Pharmacology and Molecular Sciences, The Johns Hopkins University School of Medicine, Baltimore, MD, 21205, USA



09/891865 SEARCH STRATEGY

SOURCE: Nature Structural Biology (2001), 8(1), 37-41  
 CODEN: NSBIW; ISSN: 1072-8368  
 PUBLISHER: Nature America Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Protein kinase inhibitors have applications as anticancer therapeutic agents and biol. tools in cell signaling. Based on a phosphoryl transfer mechanism involving a dissociative transition state, a potent and selective bisubstrate inhibitor for the insulin receptor tyrosine kinase was synthesized by linking ATP.gamma.S to a peptide substrate analog via a two-carbon spacer. The compd. was a high affinity competitive inhibitor against both nucleotide and peptide substrates and showed a slow off-rate. A crystal structure of this inhibitor bound to the tyrosine kinase domain of the insulin receptor confirmed the key design features inspired by a dissociative transition state, and revealed that the linker takes part in the octahedral coordination of an active site Mg2+. These studies suggest a general strategy for the development of selective protein kinase inhibitors.

IT 329783-44-0D, complexes with insulin receptor kinase

RL: PRP (Properties)

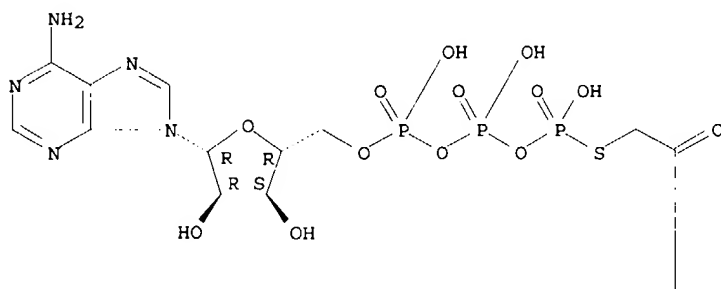
(crystal structure of bisubstrate inhibitor complexes with insulin receptor kinase)

RN 329783-44-0 CAPLUS

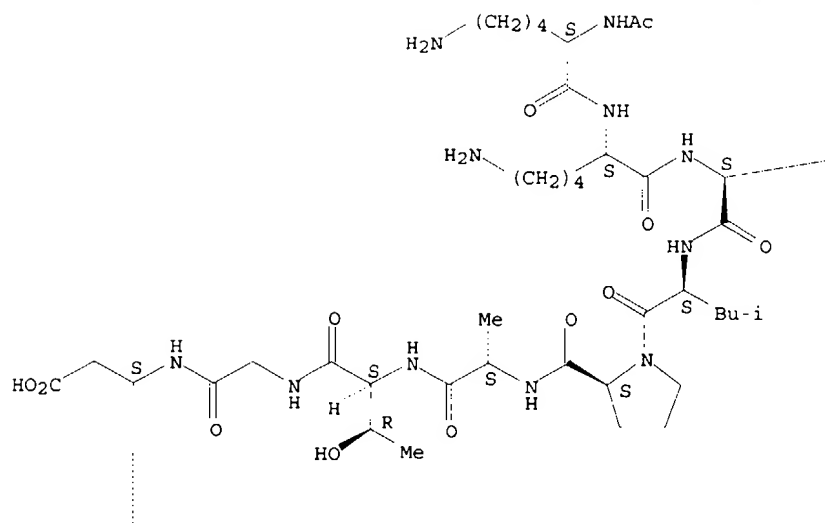
CN L-Aspartic acid, N2-acetyl-L-lysyl-L-lysyl-L-lysyl-L-leucyl-L-prolyl-L-alanyl-L-threonylglycyl-L-.alpha.-aspartyl-4-[[6-(5'-adenylyloxy)-4,6-dihydroxy-4,6-dioxido-1-oxo-5-oxa-3-thia-4,6-diphosphahex-1-yl]amino]-L-phenylalanyl-L-methionyl-L-asparaginyl-L-methionyl-L-seryl-L-prolyl-L-valylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

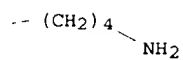
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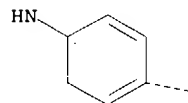
PAGE 1 - B



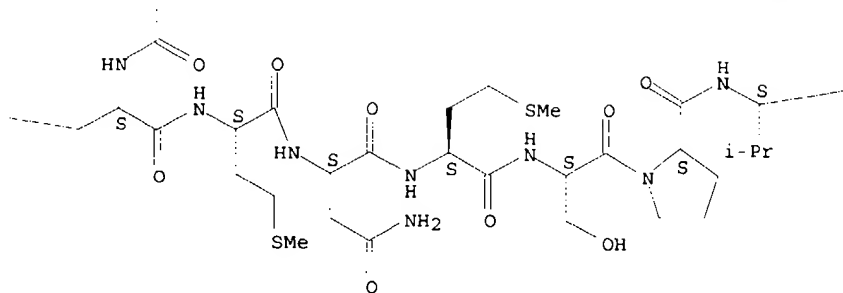
PAGE 1 - C



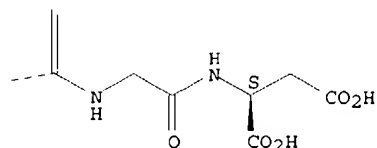
PAGE 2-A



PAGE 2-B



PAGE 2-C



RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(mechanism-based design of bisubstrate inhibitor of insulin receptor kinase)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=&gt; log y

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
9.49	158.25

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
-1.30	-1.30

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STN INTERNATIONAL LOGOFF AT 13:13:26 ON 13 NOV 2003